


**REMARKS**

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. §1.112, are respectfully requested.

By the present amendment, claims 11-13 and 26-28 have been amended to exclude "prophylactic" from the claims and claims 39 and 41 have been amended to exclude "preventing" from the claims. Furthermore, new claims 42 and 43 have been added. New claims 42 and 43 find support, at the very least, in original claims 39 and 41. Thus, by the present amendment, claims 39 and 41 have been split into method of treatment claims (i.e. amended claims 39 and 41) and method of prevention claims (i.e. new claims 42 and 43).

Claims 2-13, 15, 17-28 and 38-41 have been rejected under 35 U.S.C. §112, first paragraph, because the invention is allegedly not enabled for the prevention of diseases related to NF- $\kappa$ B and TNF- $\alpha$  using the compounds of formula I. Applicants respectfully traverse this rejection.

Initially, as noted above, the claims have been amended to separate the method of treatment claims from the method of prevention claims. Thus, claims 11-13 and 39 are now drawn to methods of treating diseases caused by the activation of NF- $\kappa$ B. Claims 26-28 and 41 are drawn to methods of treating diseases caused by the activation of TNF- $\alpha$ . Claims 2-10 and 15 are drawn to methods for inhibiting NF- $\kappa$ B. Claims 17-25, 38 and 40 are drawn to methods for inhibiting TNF- $\alpha$ . Newly added claims 42 and 43 are drawn to methods of preventing diseases caused by the activation of NF- $\kappa$ B and TNF- $\alpha$ , respectively.



The Examiner has not challenged the treatment aspect of Applicants invention or the aspect of the invention drawn to methods for inhibiting NF- $\kappa$ B or TNF- $\alpha$ , but rather only challenges the prevention aspects of the claimed invention. Thus, at the very least, pending claims 2-13, 15, 17-28 and 38-41 are in condition for allowance.

With regards to the claims drawn to methods of preventing diseases (i.e. claims 42 and 43) applicants respectfully disagree with the Examiner's position that these claims are not enabled by the specification as filed. NF- $\kappa$ B is activated by transmitting signals caused by binding of inflammatory cytokines to receptors. The activated NF- $\kappa$ B binds to expression control regions for the genes which encode iNOS, TNF- $\alpha$ , etc., which are inflammatory proteins, so as to express these proteins. The expression of these proteins worsens the inflammation. Inflammatory diseases are diseases which progressively worsen, and therefore inhibition of NF- $\kappa$ B activation will inhibit the progression of the disease, and therefore prevent worsening of the disease. Thus, in the field of inflammation, treatment and prevention cannot be distinguished as far as the mechanism of inflammation is concerned. Therefore, various diseases caused by the activation of NF- $\kappa$ B can be prevented by inhibition of NF- $\kappa$ B activation.

In light of the above remarks, applicants respectfully request withdrawal of this rejection under 35 U.S.C. § 112, first paragraph.

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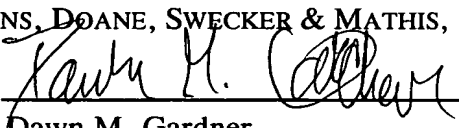
CONCLUSION

From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order and such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of this application may be expedited.

Respectfully submitted,  
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**Attachment to Amendment dated March 22, 2002**

**Marked-up Claims 11-13, 26-28, 39 and 41**

11. (Four Times Amended) The method according to claim 38 which is a [prophylactic or] treatment for inflammatory diseases.

12. (Four Times Amended) The method according to claim 38 which is a [prophylactic or] treatment for autoimmune diseases.

13. (Four Times Amended) The method according to claim 38 which is a [prophylactic or] treatment for viral diseases.

26. (Four Times Amended) The method according to claim 40 which is a [prophylactic or] treatment for inflammatory diseases.

27. (Four Times Amended) The method according to claim 40 which is a [prophylactic or] treatment for autoimmune diseases.

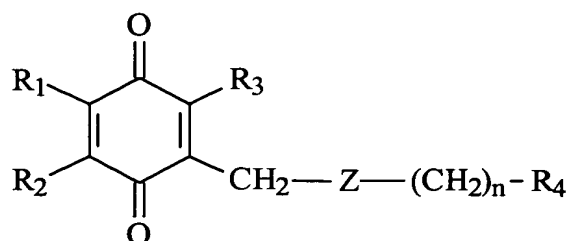
28. (Four Times Amended) The method according to claim 40 which is a [prophylactic or] treatment for viral diseases.



Attachment to Amendment dated March 22, 2002

**Marked-up Claims 11-13, 26-28, 39 and 41**

39. (Twice Amended) A method for [preventing or] treating diseases caused by the activation of NF- $\kappa$ B comprising administering to a patient a benzoquinone derivative represented by the following general formula (1):

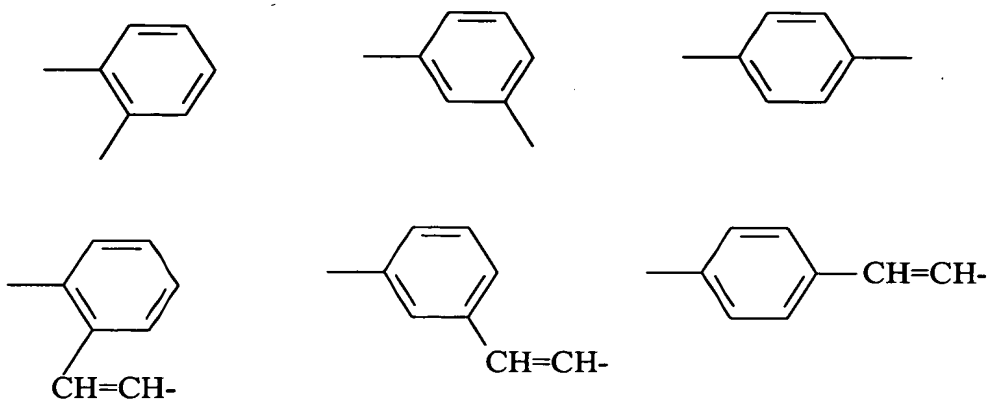


wherein

R<sub>1</sub>, R<sub>2</sub>, and R<sub>3</sub> are each independently a hydrogen atom, an alkyl group having 1 to 5 carbons, or an alkoxy group having 1 to 5 carbons;

R<sub>4</sub> is a hydrogen atom, a hydroxymethyl group, an alkyl group, or a carboxyl group which is optionally esterified or amidated;

Z is



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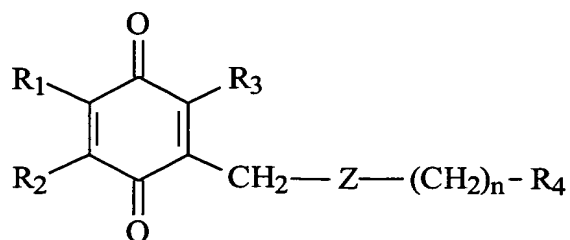
Attachment to Amendment dated March 22, 2002

**Marked-up Claims 11-13, 26-28, 39 and 41**

and, n is an integer from 0 to 6,

or its hydroquinone form, or a pharmaceutically acceptable salt thereof.

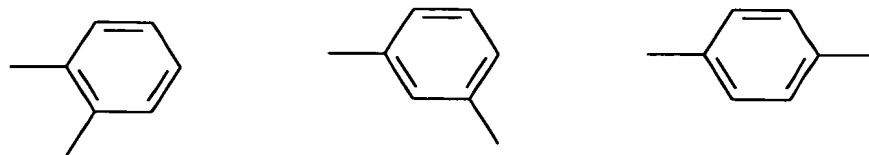
41. (Twice Amended) A method for [preventing or] treating diseases caused by the excessive production of TNF- $\alpha$  comprising administering to a patient a benzoquinone derivative represented by the following general formula (1):



wherein R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> are each independently a hydrogen atom, an alkyl group having 1 to 5 carbons, or an alkoxy group having 1 to 5 carbons;

R<sub>4</sub> is a hydrogen atom, a hydroxymethyl group, an alkyl group, or a carboxyl group which is optionally esterified or amidated;

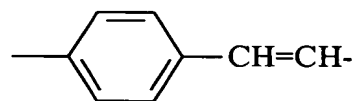
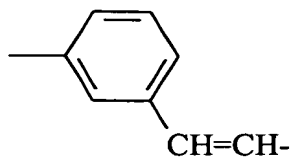
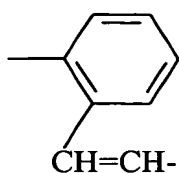
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**Attachment to Amendment dated March 22, 2002**

**Marked-up Claims 11-13, 26-28, 39 and 41**



and, n is an integer from 0 to 6,

or its hydroquinone form, or a pharmaceutically acceptable salt thereof.

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